

WHAT IS CLAIMED IS:

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1. A composition comprising a bacterial pilus to which an antigen or antigenic determinant has been attached by a covalent bond.
  2. The composition of claim 1, wherein said covalent bond is not a peptide bond.
  3. The composition of claim 1, wherein said bacterial pilus is a Type-1 pilus of Escherichia coli.
  4. The composition of claim 1, wherein pilin subunits of said Type-1 pilus comprises the amino acid sequence shown in SEQ ID NO: 146 or a sequence having at least 65, 70, 75, 80, 85, 90 or 95% sequence identity to SEQ ID NO: 146.
  5. The composition of claim 1, wherein said bacterial pilus and said antigen or antigen determinant are attached via a non-naturally occurring attachment.
  6. The composition of claim 1, wherein said attachment comprises an organizer comprising at least one first attachment site, and wherein said organizer is connected to said pilus by at least one covalent bond.
  7. The composition of claim 6, wherein said organizer is a polypeptide or a residue thereof, and wherein said second attachment site is a polypeptide or a residue thereof.
  8. The composition of claim 6, wherein said first and/or a second attachment sites comprise:

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- (a) an antigen and an antibody or antibody fragment thereto;  
(b) biotin and avidin;  
(c) strepavidin and biotin;  
(d) a receptor and its ligand;  
(e) a ligand-binding protein and its ligand;  
(f) interacting leucine zipper polypeptides;  
(g) an amino group and a chemical group reactive thereto;  
(h) a carboxyl group and a chemical group reactive thereto;  
(i) a sulfhydryl group and a chemical group reactive thereto;

or

- (j) a combination thereof.

9. The composition of claim 1, wherein said bacterial pilus and said antigen or antigenic derminant are attached by an attachment comprising interacting leucine zipper polypeptides.

10. The composition of claim 5, wherein interacting leucine zipper polypeptides are JUN and/or FOS leucine zipper polypeptides.

11. A composition comprising a bacterial pilin polypeptide to which an antigen or antigenic determinant has been attached by a covalent bond.

12. The composition of claim 11, wherein said covalent bond is not a peptide bond.

13. The composition of claim 11, wherein said polypeptide is from a Type-1 pilus of Escherichia coli.

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14. The composition of claim 11, wherein said bacterial pilin polypeptide comprises the amino acid sequence shown in SEQ ID NO:146 or a sequence having at least 65, 70, 75, 80, 85, 90 or 95% sequence identity to SEQ ID NO:146.

15. The composition of claim 11, wherein said bacterial pilin polypeptide and said antigen or antigenic determinant are attached by a non-naturally occurring attachment.

16. The composition of claim 11, wherein said attachment comprises an organizer comprising at least one first attachment site, and wherein said organizer is connected to said pilus by at least one covalent bond.

17. The composition of claim 16, wherein said organizer is a polypeptide or a residue thereof, and wherein said second attachment site is a polypeptide or a residue thereof.

18. The composition of claim 11, wherein said first and/or a second attachment sites comprise:

- (a) an antigen and an antibody or antibody fragment thereto;
  - (b) biotin and avidin;
  - (c) streptavidin and biotin;
  - (d) a receptor and its ligand;
  - (e) a ligand-binding protein and its ligand;
  - (f) interacting leucine zipper polypeptides;
  - (g) an amino group and a chemical group reactive thereto;
  - (h) a carboxyl group and a chemical group reactive thereto;
  - (i) a sulfhydryl group and a chemical group reactive thereto;
- or
- (j) a combination thereof.

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19. The composition of claim 15, wherein said attachment comprises interacting leucine zipper polypeptides.

20. The composition of claim 13, wherein said interacting leucine zipper polypeptides are JUN and/or FOS leucine zipper polypeptides.

21. A composition comprising:

(a) a non-natural molecular scaffold comprising:

(i) a core particle selected from the group consisting

of:

(1) a bacterial pilus or pilin protein; and

(2) a recombinant form of a bacterial pilus or

pilin protein; and

(ii) an organizer comprising at least one first attachment

site,

wherein said organizer is connected to said core particle by at least one covalent bond; and

(b) an antigen or antigenic determinant with at least one second attachment site, said second attachment site being selected from the group consisting of:

(i) an attachment site not naturally occurring with said antigen or antigenic determinant; and

(ii) an attachment site naturally occurring with said antigen or antigenic determinant,

wherein said second attachment site is capable of association through at least one non-peptide bond to said first attachment site; and

wherein said antigen or antigenic determinant and said scaffold interact through said association to form an ordered and repetitive antigen array.

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22. The composition of claim 21, wherein said organizer is a polypeptide or residue thereof; and wherein said second attachment site is a polypeptide or residue thereof.

23. The composition of claim 21, wherein said first and/or said second attachment sites comprise:

- (a) an antigen and an antibody or antibody fragment thereto;
- (b) biotin and avidin;
- (c) strepavidin and biotin;
- (d) a receptor and its ligand;
- (e) a ligand-binding protein and its ligand;
- (f) interacting leucine zipper polypeptides;
- (g) an amino group and a chemical group reactive thereto;
- (h) a carboxyl group and a chemical group reactive thereto;
- (i) a sulfhydryl group and a chemical group reactive thereto;

or

- (j) a combination thereof.

24. The composition of claim 21, wherein said first and/or said second attachment sites comprise interacting leucine zipper polypeptides.

25. The composition of claim 21, wherein said bacterial pilus is a Type-1 pilus of Eschericia coli.

26. The composition of claim 21, wherein pilus subunits of said type-1 pilus comprise the amino acid sequence of SEQ ID No. 146 or a sequence having at least 65, 70, 75, 80, 85, 90 or 95% sequence identity to SEQ ID NO:146.

27. The composition of claim 26, wherein said interacting leucine zipper polypeptides are the JUN and/or FOS leucine zipper polypeptides.

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28. A composition comprising:

(a) a non-natural molecular scaffold comprising:

(i) a virus-like particle that is a dimer or a multimer of a polypeptide comprising amino acids 1-147 of SEQ ID NO:158 as core particle or a sequence having at least 65, 70, 75, 80, 85, 90 or 95% sequence identity to SEQ ID NO:158; and

(ii) an organizer comprising at least one first attachment site,

wherein said organizer is connected to said core particle by at least one covalent bond; and

(b) an antigen or antigenic determinant with at least one second attachment site, said second attachment site being selected from the group consisting of:

(i) an attachment site not naturally occurring with said antigen or antigenic determinant; and

(ii) an attachment site naturally occurring with said antigen or antigenic determinant,

wherein said second attachment site is capable of association through at least one non-peptide bond to said first attachment site; and

wherein said antigen or antigenic determinant and said scaffold interact through said association to form an ordered and repetitive antigen array.

29. The composition of claim 28, wherein said organizer is a polypeptide or residue thereof, and wherein said second attachment site is a polypeptide or residue thereof.

30. The composition of claim 28, wherein said first and/or said second attachment sites comprise:

(a) an antigen and an antibody or antibody fragment thereto;

(b) biotin and avidin;

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- (c) strepavidin and biotin;
  - (d) a receptor and its ligand;
  - (e) a ligand-binding protein and its ligand;
  - (f) interacting leucine zipper polypeptides;
  - (g) an amino group and a chemical group reactive thereto;
  - (h) a carboxyl group and a chemical group reactive thereto;
  - (i) a sulfhydryl group and a chemical group reactive thereto;
- or
- (j) a combination thereof.

31. The composition of claim 30, wherein said first attachment site is an amino group and said second attachment site is a sulfhydryl group.

32. The composition of claim 30, wherein said virus-like particle and said antigen or antigenic determinant are attached by an attachment comprising interacting leucine zipper polypeptides.

33. The composition of claim 32, wherein said interacting leucine zipper polypeptides are JUN and/or FOS polypeptides.

34. A composition comprising:

- (a) a non-natural molecular scaffold comprising:
  - (i) Hepatitis B virus capsid protein comprising an amino acid sequence selected from the group consisting of:
    - (1) the amino acid sequence of SEQ ID NO:89;
    - (2) the amino acid sequence of SEQ ID NO:90;
    - (3) the amino acid sequence of SEQ ID NO:93;
    - (4) the amino acid sequence of SEQ ID NO:98;
    - (5) the amino acid sequence of SEQ ID NO:99;

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- 102;
- (6) the amino acid sequence of SEQ ID NO:
- (7) the amino acid sequence of SEQ ID NO:
- 104;
- (8) the amino acid sequence of SEQ ID
- NO:105;
- (9) the amino acid sequence of SEQ ID
- NO:106;
- (10) the amino acid sequence of SEQ ID
- NO:119;
- (11) the amino acid sequence of SEQ ID
- NO:120;
- (12) the amino acid sequence of SEQ ID
- NO:123;
- (13) the amino acid sequence of SEQ ID
- NO:125;
- (14) the amino acid sequence of SEQ ID
- NO:131;
- (15) the amino acid sequence of SEQ ID
- NO:132;
- (16) the amino acid sequence of SEQ ID
- NO:134;
- (17) the amino acid sequence of SEQ ID
- NO:157; and
- (18) the amino acid sequence of SEQ ID
- NO:158; and

(ii) an organizer comprising at least one first attachment site,

wherein said organizer is connected to said core particle by at least one covalent bond; and

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(b) an antigen or antigenic determinant with at least one second attachment site, said second attachment site being selected from the group consisting of:

(i) an attachment site not naturally occurring with said antigen or antigenic determinant; and

(ii) an attachment site naturally occurring with said antigen or antigenic determinant,

wherein said second attachment site is capable of association through at least one non-peptide bond to said first attachment site; and

wherein said antigen or antigenic determinant and said scaffold interact through said association to form an ordered and repetitive antigen array.

35. The composition of claim 34, wherein said organizer is a polypeptide or residue thereof,

wherein said second attachment site is a polypeptide or residue thereof, and

wherein said first attachment site is a lysine residue and said second attachment site is a cysteine residue.

36. The composition of claim 34, wherein one or more cysteine residues of said Hepatitis B virus capsid protein have been either deleted or substituted with another amino acid residue.

37. The composition of claim 34, wherein said first and/or said second attachment sites comprise:

- (a) an antigen and an antibody or antibody fragment thereto;
- (b) biotin and avidin;
- (c) strepavidin and biotin;
- (d) a receptor and its ligand;
- (e) a ligand-binding protein and its ligand;

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- (f) interacting leucine zipper polypeptides;
- (g) an amino group and a chemical group reactive thereto;
- (h) a carboxyl group and a chemical group reactive thereto;
- (i) a sulfhydryl group and a chemical group reactive thereto;

or

- (j) a combination thereof.

38. The composition of claim 36, wherein the cysteine residues corresponding to amino acids 48 and 107 in SEQ ID NO:134 have been either deleted or substituted with another amino acid residue.

39. The composition of claim 37, wherein said Hepatitis B virus capsid protein and said antigen or antigenic determinant are attached by an attachment comprising interacting leucine zipper polypeptides.

40. The composition of claim 39, wherein said interacting leucine zipper polypeptides are FOS and/or JUN polypeptides.

41. The composition of any one of claims 28, 34, 35, 36 and 38, wherein said antigen is selected from the group consisting of:

- (a) an antigen suited to induce an immune response against bacteria,
- (b) an antigen suited to induce an immune response against viruses,
- (c) an antigen suited to induce an immune response against parasites,
- (d) an antigen suited to induce an immune response against cancer cells,
- (e) an antigen suited to induce an immune response against allergens,

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(f) an antigen suited to induce an immune response in a farm animals, and

(g) a protein suited to induce an immune response in a pet.

42. The composition of claim 41, wherein the antigen is a protein, polypeptide, or a fragment thereof.

43. The composition of claim 41, wherein said antigen induces an immune response against one or more allergens.

44. The composition of claim 41, wherein said antigen is:

- (a) a recombinant protein of HIV,
- (b) a recombinant protein of Influenza virus,
- (c) a recombinant protein of Hepatitis C virus,
- (d) a recombinant protein of Toxoplasma,
- (e) a recombinant protein of Plasmodium falciparum,
- (f) a recombinant protein of Plasmodium vivax,
- (g) a recombinant protein of Plasmodium ovale,
- (h) a recombinant protein of Plasmodium malariae,
- (i) a recombinant protein of breast cancer cells,
- (j) a recombinant protein of kidney cancer cells,
- (k) a recombinant protein of prostate cancer cells,
- (l) a recombinant protein of skin cancer cells,
- (m) a recombinant protein of brain cancer cells,
- (n) a recombinant protein of leukemia cells,
- (o) a recombinant profiling,
- (p) a recombinant protein of bee sting allergy,
- (q) a recombinant protein of nut allergy,
- (r) a recombinant protein of food allergies,
- (s) a recombinant protein of asthma, or

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- (t) a recombinant protein of Chlamydia.

45. The composition of any one of claims 1, 11 and 21, wherein said antigen is selected from the group consisting of:

- (a) an antigen suited to induce an immune response against bacteria,  
viruses,  
parasites,  
cancer cells,  
animals, and  
and  
(g) any other antigen involved in a pathophysiological context.

46. The composition of claim 45, wherein the antigen is a protein, a polypeptide, or a fragment thereof.

47. The composition of any one of claims 1, 11 or 21, wherein said antigen is:

- (a) a recombinant protein of HIV,  
(b) a recombinant protein of Influenza virus,  
(c) a recombinant protein of Hepatitis C virus,  
(d) a recombinant protein of Toxoplasma,  
(e) a recombinant protein of Plasmodium falciparum,  
(f) a recombinant protein of Plasmodium vivax,  
(g) a recombinant protein of Plasmodium ovale,

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- (h) a recombinant protein of *Plasmodium malariae*,
- (i) a recombinant protein of breast cancer cells,
- (j) a recombinant protein of kidney cancer cells,
- (k) a recombinant protein of prostate cancer cells,
- (l) a recombinant protein of skin cancer cells,
- (m) a recombinant protein of brain cancer cells,
- (n) a recombinant protein of leukemia cells,
- (o) a recombinant profiling,
- (p) a recombinant protein of *Chlamydia*.

48. A pharmaceutical composition comprising the composition of any one of claims 1, 11, 21, 28, 34, 35, 36, 38, 41 or 44, and a pharmaceutically acceptable carrier.

49. A vaccine composition comprising the composition of any one of claims 1, 11, 21, 28, 34, 35, 36, 38, 41 or 44.

50. The vaccine composition of claim 49, further comprising at least one adjuvant.

51. A method of immunizing, comprising administering to a subject the vaccine composition of claim 49 or 50.

52. The method of claim 51, wherein said administering produces an immune response.

53. The method of claim 51, wherein said administering produces a humoral immune response.

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54. The method of claim 51, wherein said administering produces a cellular immune response.

55. The method of claim 51, wherein said administering produces a humoral immune response and a cellular immune response.

56. The method of claim 51, wherein said administering produces a protective immune response.

57. A method of making the composition of claim 1, comprising combining said pilus and said antigen or antigenic determinant, wherein said pilus and said antigen or antigenic determinant interact to form an antigen array.

58. The method of claim 57, wherein said antigen array is ordered and/or repetitive.

59. A method of making the composition of claim 11, comprising combining said pilin polypeptide and said antigen or antigenic determinant, wherein said pilin polypeptide and said antigen or antigenic determinant interact to form an antigen array.

60. The method of claim 59, wherein said antigen array is ordered and/or repetitive.

61. A method of making the composition of claim 21, 28, 34, 35, 36 or 38, comprising combining said non-natural molecular scaffold and said antigen or antigenic determinant, wherein said non-natural molecular scaffold and said antigen or antigenic determinant interact to form an antigen array.

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62. The method of claim 61, wherein said antigen array is ordered and/or repetitive.

63. A composition comprising:

(a) a non-natural molecular scaffold comprising:

(i) a core particle selected from the group consisting

of:

(1) a bacterial pilus; and

(2) a recombinant form of a bacterial pilus or

pilin protein; and

(ii) an organizer comprising at least one first attachment

site,

wherein said organizer is connected to said core particle by at least one covalent bond; and

(b) an antigen or antigenic determinant with at least one second attachment site, said second attachment site being selected from the group consisting of:

(i) an attachment site not naturally occurring with said antigen or antigenic determinant; and

(ii) an attachment site naturally occurring with said antigen or antigenic determinant,

wherein said second attachment site is capable of association through at least one non-peptide bond to said first attachment site;

wherein said antigen or antigenic determinant and said scaffold interact through said association to form an ordered and repetitive antigen array, and

wherein said antigen or antigenic determinant is selected from the group consisting of an influenza M2 peptide, the GRA2 polypeptide, the DP178c peptide, the tumor necrosis factor polypeptide, a tumor necrosis factor peptide, the B2 peptide, the D2 peptide, and the A $\beta$  peptide.

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64. The composition of claim 63, wherein said antigen or antigenic determinant is the influenza M2 peptide or variants thereof.

65. The composition of claim 63, wherein said antigen or antigenic determinant is the GRA2 polypeptide.

66. The composition of claim 63, wherein said antigen or antigenic determinant is the DP178c peptide.

67. The composition of claim 63, wherein said antigen or antigenic determinant is the tumor necrosis factor polypeptide.

68. The composition of claim 63, wherein said antigen or antigenic determinant is a tumor necrosis factor peptide.

69. The composition of claim 63, wherein said antigen or antigenic determinant is the B2 peptide.

70. The composition of claim 63, wherein said antigen or antigenic determinant is the D2 peptide.

71. The composition of claim 63, wherein said antigen or antigenic determinant is the A $\beta$  peptide.

72. The composition of claim 63, wherein said organizer is a polypeptide or residue thereof, and wherein said second attachment site is a polypeptide or residue thereof.

73. The composition of claim 63, wherein said first and/or said second attachment sites comprise:

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- (a) an antigen and an antibody or antibody fragment thereto;  
(b) biotin and avidin;  
(c) strepavidin and biotin;  
(d) a receptor and its ligand;  
(e) a ligand-binding protein and its ligand;  
(f) interacting leucine zipper polypeptides;  
(g) an amino group and a chemical group reactive thereto;  
(h) a carboxyl group and a chemical group reactive thereto;  
(i) a sulfhydryl group and a chemical group reactive thereto;  
(j) a combination thereof.

or

74. The composition of claim 63, wherein said first and/or said second attachment sites comprise interacting leucine zipper polypeptides.

75. The composition of claim 63, wherein said bacterial pilus is a Type-1 pilus of Eschericia coli.

76. The composition of claim 63, wherein pilus subunits of said type-1 pilus comprise the amino acid sequence of SEQ ID No. 146 or a sequence having at least 65, 70, 75, 80, 85, 90 or 95% sequence identity to SEQ ID NO:146.

77. The composition of claim 63, wherein said interacting leucine zipper polypeptides are the JUN and/or FOS leucine zipper polypeptides.

78. A vaccine composition comprising the composition of claim 63 or claim 43.

79. A method of immunizing, comprising administering to a subject the vaccine composition of claim 49 or 50.

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80. The method of claim 79, wherein said administering produces an immune response.

81. A method of making the composition of claim 63, comprising combining said non-natural molecular scaffold and said antigen or antigenic determinant, wherein said non-natural molecular scaffold and said antigen or antigenic determinant interact to form an antigen array.

82. The method of claim 81, wherein said antigen array is ordered and/or repetitive.

83. A method of immunizing, comprising administering the composition of any one of claims 1, 11, 21, 49 or 50 to a subject, wherein for inducing a Th2 response, wherein said administering produces a Th2 response that is specific for said antigen or antigenic determinant.

84. The method of claim 83, wherein antibodies specific for said antigen or antigenic determinant of a subtype corresponding to the Th2 subtype are induced in the subject.

85. The method of claim 83, wherein the subject does not generate a Th1 response that is specific for said pilus, said pilin polypeptide, or said antigen or antigenic determinant.

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